## REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 1-6, 10-16, and 19-27 are pending in the application. Claims 1, 5 and 16 have been amended to address formal matters. New claims 19-27 have been added. Support for new claims 19-27 may be found generally throughout the specification and in the original claims. Claim 9 has been canceled.

In the outstanding Official Action, the specification was objected to for reciting Examples 5 and 6 but not reciting an Example 4. However, the specification has been amended to correct this informality. Applicants thank the Examiner for his suggestion as how to overcome this objection.

Claims 5 and 16 were objected for allegedly containing several informalities. Claims 5 and 16 have been amended as suggested by the Examiner to overcome the objections to those claims. Again, applicants thank the Examiner for his suggestion as how to overcome the objections.

Claims 1-6 and 8-16 were rejected under 35 USC §112, first paragraph, for allegedly failing to satisfy the written description requirement. This rejection is traversed.

In imposing the rejection, the Official Action notes that original claim 7 specifically recited a method "according to

any one of claims 1-3, in which the label is neutralized after step d)". In addition, the Official Action notes that page 45 of the specification states that "the label is neutralized after step d)". Accordingly, the Official Action concludes that the specification and original claim 7 only teach neutralization after step d). Applicants respectfully disagree.

Claim 7 was a dependent claim. Under the doctrine of claim differentiation, it is clear that this embodiment is a preferred embodiment. Indeed, one skilled in the art would understand that two claims in the same patent application would not have the identical scope. Moreover, it is clear that the embodiment is preferred or a "further embodiment" (see page 4, last paragraph).

In view of the above, applicants respectfully request that the rejection be withdrawn.

Claims 1-6, 8-13 and 16 were rejected under 35 USC \$103(e) as allegedly being unpatentable over KAWASHIMA et al. in view of URDEA et al. Claims 11-12 were rejected under 35 USC \$103(a) as allegedly being unpatentable over KAWASHIMA et al. in view of URDEA et al. and further in view of VERDINE. Claim 14 was rejected under 35 USC \$103(a) as allegedly being unpatentable over KAWASHIMA et al. in view of URDEA et al. and further in view of UEMORI et al. Claim 15 was rejected under 35 USC \$103(a) as allegedly being unpatentable over KAWASHIMA et al. in view of

URDEA et al. and further in view of LEE et al. These rejections are traversed.

the recitations of determining the type of nucleotide added to the primer and neutralizing the label by adding a label-interacting agent or by bleaching "after" the preceding step. In addition, the claim states that the label neutralization after determining the type of the nucleotide is required before an additional primer extension is added. Step d) now recites repeating step c). Thus, claim 1 stand in contrast to KAWASHIMA in that i) neutralization of the label occurs in each cycle and there is a cleavable bond between the nucleotide and the label.

Indeed, as already noted, KAWASHIMA discloses that different nucleic acid molecules present at different locations can be sequenced in parallel. In particular, KAWASHIMA utilizes primers that are annealed to the nucleic acid molecules. Each location can then be provided with a nucleic acid polymerase and a nucleotide. It can then be determined whether or not the nucleotide has been used in primer extension and the process can be repeated.

As noted at page 6, lines 18-27, one of the advantages of the method of KAWASHIMA is that there is no need to remove a label from a nucleotide chain. If labels are removed, they are only removed periodically, not after each detection step.

Applicants also maintain that the passage at page 18, lines 9-26 merely states that after several steps of sequencing that it may be desirable to remove a label. KAWASHIMA does not disclose or suggest claimed steps c) or d).

Moreover, even if one skilled in the art were to combine the teachings of KAWASHIMA with URDEA or the other publications, one would still not obtain the claimed invention.

URDEA relates to labelled nucleotides where the fluorescent label is linked to the nucleotide with a cleavable disulfide linker. URDEA does not relate to sequencing methods.

VERDINE teaches the attachment of molecules to nucleotides using disulfide links. However, there is no suggestion of removing a label from a nucleotide chain as recited in the claimed invention.

UEMORI relates to a DNA polymerase. UEMORI does  $\underline{\text{not}}$  teach a method as recited in the claimed invention.

LEE discloses a method for primer extension using fluorescent compounds for labels. There is no suggestion of a method utilizing step d) as recited in the claimed invention.

The Examiner's attention is also respectfully directed to claims 19-27, which recite that step c) "consists of" several steps, which is plainly not taught by the prior art.

Thus, while the outstanding Official Action cites to URDEA, VERDINE, UEMORI and LEE, none of these publications disclose or suggest such a feature.

As a result, applicants respectfully request that the obviousness rejections be withdrawn.

As to the non-statutory obviousness-type double patenting rejection, the Examiner's attention is respectfully directed to MPEP §804 (I) (B)1. MPEP §804 (I) (B)1 provides that if a "provisional" non-statutory obviousness type double patenting rejection is the only rejection remaining in the earlier filed of two pending applications, while the later-filed applicant is rejectable on other grounds, the Examiner should withdraw that rejection to permit the earlier-filed application to issue as patent without a terminal disclaimer. As the present application was filed earlier than copending application No. 10/529,352, applicants note that the double patenting rejection should not prevent the present application from allowance and passage to issue. Thus, as all of the rejections identified above have been properly addressed, applicants believe that the present application is in condition for allowance at the time of the next Official Action.

In view of the present amendment and the foregoing remarks, therefore, applicants believe that the present application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

Docket No. 1501-1276 Application No. 10/510,107

overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. \$ 1.16 or under 37 C.F.R. \$ 1.17.

Respectfully submitted,

YOUNG & THOMPSON

Philip A. DuBois, Reg. No. 50,696

209 Madison Street, Suite 500

Alexandria, VA 22314

Telephone (703) 521-2297

Telefax (703) 685-0573

(703) 979-4709

PD/mjr